

- 1) A method of treating hemophilia, said method comprising
  - a) aerosolizing a Factor IX (F.IX), wherein the aerosolized F.IX:
    - i) has a mass median aerodynamic diameter (MMAD) of between 2 and 4  $\mu\text{m}$ , has a fine particle fraction percent less than 3.3  $\mu\text{m}$  ( $\text{FPF}_{\% < 3.3 \mu\text{m}}$ ) of at least 50%,
    - ii) is at least 90% monomeric,
    - iii) wherein the after-aerosolization activity/pre-aerosolization activity is at least 80%;  
and
    - iv) is a dry powder having less than 10% water (wt/wt);
  - b) inhaling the aerosolized F.IX and allowing the aerosolized F.IX to deposit in the lung;
  - c) followed by exhalation.
- 2) The method of claim 1, wherein the MMAD is 2.8 to 3.6  $\mu\text{m}$ , the  $\text{FPF}_{\% < 3.3 \mu\text{m}}$  is at least 60%, the monomer content is at least 95% and the after-aerosolization activity/pre-aerosolization activity is at least 90%.
- 3) The method of claim 1, wherein the MMAD is about 3-3.5  $\mu\text{m}$ , the  $\text{FPF}_{\% < 3.3 \mu\text{m}}$  is at least 64%, the monomer content is at least 97%, and the after-aerosolization activity/pre-aerosolization activity is at least 95%.
- 4) The method of claim 1, wherein the F.IX is aerosolized without alcohol.
- 5) The method of claim 1, wherein the F.IX is recombinant.
- 6) The method of any of claims 1 through 5, wherein the F.IX comprises a tri-leucine excipient.
- 7) The method of claim 6, wherein the tri-leucine/F.IX ratio is 0.5-1.5wt/wt.
- 8) A method of treating hemophilia, said method comprising the inhalation of aerosolized, dry Factor IX (F.IX), wherein the aerosolized dry F.IX:
  - a) comprises a surface active di- or tri-peptide, b) has a MMAD of between 2.8-3.5  $\mu\text{m}$ ,
  - c) an  $\text{FPF}_{\% < 3.3 \mu\text{m}}$  of greater than 60%, d) a monomer content of at least 95%, e) the after-

aerosolization activity/pre-aerosolization activity is at least 80%, and f) less than 10% water.

- 9) The method of claim 8, wherein the MMAD is about 3-3.5  $\mu\text{m}$ , the  $\text{FPF}_{\% < 3.3 \mu\text{m}}$  is at least 64%, the after-aerosolization activity/pre-aerosolization activity is at least 90%; the monomer content is at least 97% and the water content is less than 5%.
- 10) The method of claim 8, wherein the F.IX does not contain alcohol.
- 11) The method of claim 8, wherein the F.IX is recombinant.
- 12) The method of any of claims 8 through 11, wherein the F.IX comprises a tri-leucine excipient.
- 13) The method of claim 6, wherein the tri-leucine/F.IX ratio is 0.5-1.5wt/wt.
- 14) A method of preventing hemophilic bleeding in advance of a hemophilic assault, said method comprising
  - a) aerosolizing a Factor IX (F.IX), wherein the aerosolized F.IX:
    - i) has a mass median aerodynamic diameter (MMAD) of between 2 and 4  $\mu\text{m}$ ,
    - ii) has a fine particle fraction percent less than 3.3  $\mu\text{m}$  ( $\text{FPF}_{\% < 3.3 \mu\text{m}}$ ) of at least 50%,
    - iii) is at least 90% monomeric,
    - iv) wherein the after-aerosolization activity/pre-aerosolization activity is at least 80%;  
and
    - v) is a dry powder having less than 10% water (wt/wt);
  - b) inhaling the aerosolized F.IX at least once per week and allowing the aerosolized F.IX to deposit in the lung;
  - c) followed by exhalation.

- 15) The method of claim 14, wherein the inhalation is bi-weekly.
- 16) The method of claim 14, wherein the inhalation is every 2 to 3 days.
- 17) A composition comprising aerosolizable dry F.IX having, when aerosolized an MMAD between 2 and 4  $\mu\text{m}$ , an  $\text{FPF}_{\% < 3.3 \mu\text{m}}$  of at least 50%, an emitted dose (ED) of at least 50%, a monomer content of at least 95%, wherein the after-aerosolization activity/pre-aerosolization activity is at least 80%, less than 10% water, and a surface active di- or tri-peptide excipient, but does not have ethanol.
- 18) The composition of claim 17, wherein the MMAD is between 2.8 and 3.6  $\mu\text{m}$ , the ED is at least 60%, the after-aerosolization activity/pre-aerosolization activity is at least 95%, the  $\text{FPF}_{\% < 3.3 \mu\text{m}}$  is at least 65% and less than 5% water.
- 19) The composition of claim 17, wherein the MMAD is between 3 and 3.5  $\mu\text{m}$ , the  $\text{FPF}_{\% < 3.3 \mu\text{m}}$  is at least 64%, the ED is at least 80%, wherein the after-aerosolization activity/pre-aerosolization activity is at least 95%, the monomer content is at least 97% and the water content is less than 5%.
- 20) A blister pack containing F.IX, wherein the blister pack is waterproof and contains F.IX that is at least 90% monomeric and has less than 10% (wt/wt) water and a surface active di- or tri-peptide excipient, but does not have ethanol.
- 21) The blister pack of claim 20, wherein the F.IX is at least 95% monomeric and has less than 5% (wt/wt) water and the excipient is a dileucyl or a tri-leucine.
- 22) The blister pack of claim 20, wherein the F.IX is at least 97% monomeric and has less than 5% (wt/wt) water and the excipient is tri-leucine.
- 23) The blister pack of any of claims 20 to 22, wherein the F.IX is recombinant F.IX.
- 24) A dry powdered F.IX comprising a biologically active recombinant Factor IX that is at least 90% monomeric and has less than 10% water, and a surface active di- or tri-peptide excipient, but does not have ethanol.

- 25) The dry powdered F.IX of claim 24, wherein the excipient is tri-leucine.
- 26) The dry powdered F.IX of claim 25, wherein there ratio of F.IX to excipient is 0.2-5.0/1.
- 27) A composition comprising dry, dispersible powder and a solid content of about 50 wt% glycosylated F.IX, about 40 wt% trileucine and about 10 wt% buffer.
- 28) A composition comprising dry, dispersible powder and a solid content of 40-60 wt% glycosylated F.IX, 40-60 wt% trileucine and 0-10 wt% buffer.